2173-Pos Board B159
Chromatin Ordering in the SV40 Virus
Gadiel Saper, Stanislav Kler, Ariella Oppenheim, Uri Raviv, **Daniel Harries**.
The Simian Virus 40 (SV40) is composed of an outer shell formed from capsid proteins, enveloping a minichromosome that is made of double stranded DNA wound around ca. 20 nucleosomes. In contrast to many bacteriophages and RNA viruses, the structure and order of the packaged viral chromatin has remained elusive. Using small angle x-ray diffraction as well as computer modeling, we show that a unique ordering of the nucleic acid emerges, indicating at least two concentric shells of higher minichromosomal electron density. Analysis shows that packaging can be explained by considering the competition of interactions between disk-like nucleosomal particles that favor columnar ordering versus wall-nucleosome interactions that tend to align particles with the capsid interior.

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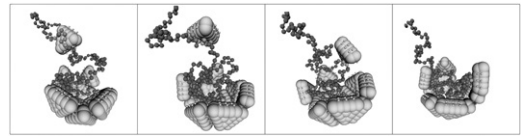
Assembly of the Adenoviral IVa2 and L4-22K Proteins on a Viral DNA Packaging Sequence
Teng-Chieh (Jay) Yang.
A critical step in the viral life cycle of ds DNA viruses such as Adenovirus, Bacteriophage lambda and Herpes, is the encapsidation of the viral genome. In human Adenovirus, this step is initiated by the assembly of two viral proteins, called IVa2 and L4-22K, onto conserved sequences within the viral genome. Genetic studies have shown that a critical feature of these sequences is that multiple copies are present, which strongly suggests that heterotropic cooperative interactions between these two proteins control the viral decision to initiate the genome encapsidation reaction. Precise control of the viruses decision to begin to manufacture viral particles is required to optimize virus particle numbers. Here we apply rigorous hydrodynamic and thermodynamic approaches to investigate the equilibrium mechanism of assembly onto viral DNA. Based on these data, we propose a detailed biochemical model which provides, for the first time, a predictive understanding of the regulation of viral DNA packaging.

2175-Pos Board B161
Assembly of an Unenveloped Icosahedral RNA Viruses using Coarse-Grained Models
Mustafa B. Boz, Thanawadee Preeprem, Stephen C. Harvey.
We investigate the assembly of Satellite Tobacco Mosaic Virus (STMV) in a coarse-grained model. We use multi-level coarse-grained representations to decrease the computational expenses and adequately represent the different parts of the viral structure. The RNA coarse grain model was generated from a combination of an idealized RNA secondary structure based on the X-ray crystal and a proposed tRNA-like secondary structure at the 3' end. The RNA model has one pseudo atom (bead) per residue. The coarse-grained model for the capsid contains 20 triangular units, each of which also contains three flexible positively charged protein tails. The assembly process as well as the stability of the virus mainly depends on RNA-protein and protein-protein interactions. The protein tails are attracted to the RNA by electrostatic interactions while the capsid proteins are weakly attracted with each other by hydrophobic interactions. We modeled RNA-protein interactions with a Debye-Hückel potential and protein-protein interaction with a Lennard-Jones potential. We varied values of these two interactions to find regions where the virus is stable and will self-assemble, and construct a phase diagram of viral stability. Finally we investigated the assembly of the virus using molecular dynamics. These simulations help us understand the individual roles of these two interactions on viral assembly.

2176-Pos Board B162
Computational Modeling of DNA Ejection from Bacteriophages to Bacterial Cells
Anton S. Petrov, Stephen C. Harvey.
Ejection of DNA from bacteriophages to bacterial cells is a spontaneous process (at least in the initial stage) and does not require the aid of an external motor. However, packaging experiments and simulations predict that the internal pressure drops to nearly zero if the amount of DNA inside the bacteriophage is less than 50%. Thus, the internal pressure itself is believed to be incapable of driving the ejection of the remaining genome.
We developed a coarse-grained model to study DNA ejection, which includes DNA represented by beads on a string, a capsid treated as a spherical constraint, a channel, and a bacterial cell modeled as a large sphere. The ejection simulations were carried out using a Langevin Dynamics protocol to account for the viscosity of the medium inside the bacterial cell. Additionally, we applied a local force to mimic the osmotic pressure inside the cell. The model of DNA ejection is further improved to account for the explicit presence of macromolecules inside bacterial cells.
We found that in all cases the ejection force drops to nearly zero as the initial fraction of 50%-60% of DNA is ejected. However, at low viscosity and/or low (or zero) osmotic pressure, the force increases up to a few piconewtons as the remaining fraction of DNA is ejected. This additional force is due to the conformational constraints of the ejected DNA. The force increase is not seen in case of large viscosity and/or applied pressure of 2-4 atm. Explicit crowding agents inside the cell affected both the thermodynamics and kinetics of ejection: because only a certain volume fraction was available for DNA, the ejection force was found to be smaller compared to the case with continuum viscous media. Smaller force resulted in longer ejection times.

2177-Pos Board B163
Order Parameters for Multiscale Simulation of Bio-Nanosystems
Abhishek Singharoy, Peter Ortoleva.
Order Parameters (OPs) characterizing the structure and organization of bio-nanosystems (BNSs) are presented. Deductive all-atom multiscale techniques imply that structural transitions in several BNSs can be simulated via the slow, temporal OP dynamics, which co-evolves with a quasi-equilibrium probability density for rapidly fluctuating atomic configurations. This yields a force-field based algorithm that allows for all-atom BNS simulations with high CPU efficiency. Salient features of a set of OPs including their construction, emergence and dynamical completeness are discussed. These are critical in probing the free-energy landscapes underlying structural transitions. The computational algorithm is implemented via a software, denoted SimNanoWorld, that we demonstrate in applications to macromolecules and macromolecular assemblies. This includes simulating the dynamics of viral RNA and RNA-protein complexes in Satellite Tobacco Mosaic Virus (STMV) over a range of electrolytes (1:1 and 2:1) and temperatures (300K-600K). Another example demonstrates the application of OPs in probing the stability and immunogenicity of a T =1 Human Papillomavirus (HPV) L1-protein Virus-like Particle (VLP). Prospects of computer-aided vaccine design will be discussed.

2178-Pos Board B164
Dynamic Encapsidation of a Flexible Polymer by an Icosahedral Virus
Oren M. Elrad, Michael F. Hagan.
The coat proteins of many viruses spontaneously form icosahedral capsids around nucleic acids or other polymers, but the mechanism of this encapsulation process is incompletely understood. Elucidating the role of the packaged polymer in capsid formation could promote biomedical efforts to block viral replication and enable use of capsids in nanomaterials applications. To this end, we perform Brownian dynamics on a coarse-grained model that describes the assembly of an icosahedral capsid around a flexible polymer. The simulations enable experimentally testable predictions for the results of the assembly reaction as a function of experimentally accessible parameters such as polymer length, polymer-protein stoichiometry, and solution conditions. Several of the capsid morphologies that assemble around longer than optimal polymers resemble structures which have been seen experimentally. Furthermore, the simulations demonstrate that experimental control parameters dictate the mechanism by which assembly occurs. Under some conditions the polymer actively promotes its encapsulation through cooperative polymer-protein motions, resulting in an assembly mechanism entirely unlike those seen for empty capsid assembly. We also explore the role of polymer secondary structure on assembly efficiency.



2179-Pos Board B165
Learning Physical Parameters of Capsid Assembly Systems from Indirect Measures of Assembly Progress
M. Senthil Kumar, Gregory Smith, Lu Xie, Rupinder P. Khandpur, **Russell Schwartz**.
Theoretical models and simulation methods have played important roles in understanding virus capsid assembly, providing key insights into possible modes and pathways of assembly, the physical mechanisms by which these are controlled, and potential sources of off-pathway assembly and the means by which they may be avoided. These theoretical and simulation studies have, however, traditionally been limited in their ability to draw conclusions about specific capsid assembly systems, largely because the theoretical models are controlled by physical parameters (e.g., binding rates), that cannot be analytically determined from any available experimental data source. Much of the seminal work on theoretical models of capsid assembly has therefore been confined either to looking at highly simplified models of